

Single dose treatment of vaginal candidosis: Comparison of clotrimazole and isoconazole

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SUMMARY The therapeutic efficacy of a single dose 500 mg tablet of clotrimazole was compared with two 300 mg tablets of isoconazole in an open randomised study of 100 patients with vaginal candidosis confirmed by mycological culture. One week after treatment 100% of the clotrimazole treated patients and 98% of the isoconazole treated group gave mycologically negative results. Five weeks after treatment these figures were 74% and 78% respectively, showing that both regimens were equally effective.

Introduction

Vaginal candidosis is a widespread gynaecological problem among women of child bearing age. Since the introduction of effective antifungal agents, various regimens of local treatment with pessaries, tablets, creams, tampons, and even foaming pessaries have been tried. These have varied from 14 day courses of nystatin¹ and 15 day courses of miconazole impregnated tampons² to a three day course of clotrimazole vaginal tablets. The cure rates in these trials have ranged from 97.4%² to 89.4%³ one month after treatment. Several attempts have been made to assess the relationship between ano-rectal (colonic candida) and vaginal candidosis.^{1,4,5} Combined oral and vaginal treatment, however, has proved no more effective in the long term than local treatment.

Over the past few years it has become increasingly evident that the success of any treatment depends on patient compliance.⁶ Attempts have been made to encourage compliance by shortening the duration of treatment. This trend has culminated in the development of a single dose 500 mg clotrimazole pessary which can be inserted by the clinician, so ensuring total patient compliance.^{7,8} Two 300 mg isoconazole pessaries have also been shown to be effective as a single dose regimen for treating vaginal candidosis.⁹ We therefore carried out a comparison of these two single dose regimens.

Patients and methods

Women over the age of 16 years who presented at a clinic of genitourinary medicine with symptoms and

signs of acute vaginal candidosis were, with their verbal consent, included in an open, randomised trial using one 500 mg vaginal tablet of clotrimazole or two 300 mg tablets of isoconazole. Patients who had no history of vaginal candidosis during the previous three months, had a high vaginal swab which was culture positive for *Candida albicans*, and had no concomitant or mixed genital infections with *Neisseria gonorrhoeae*, *Trichomonas vaginalis*, herpes simplex virus, or *Gardnerella vaginalis* were included in the trial. Patients were excluded if they had been treated with any vaginal topical agent in the previous four weeks, were suspected of being sensitive to any of the imidazole group of drugs, were thought unlikely to cooperate with the requirements of the study, or were menstruating at the time of examination. Pregnant women were also excluded.

Patients fulfilling the criteria for admission to the trial were examined by the investigator and allocated a trial number. At this stage, the following were recorded: stage of menstrual cycle; antimycotic treatment in the past year; dates of any previous attacks of vaginal candidosis; possible predisposing factors including accompanying disease and drugs, (diabetes, immunodeficiency diseases, iron or zinc deficiency, oral contraceptive use or oral steroid use, and recent use of antibiotics); duration of present infection; severity of symptoms of discharge, irritation, and burning according to a four point scale; and severity of signs of vulvitis, vaginitis, cervicitis, and discharge using a four point scale.

Two swabs were taken from the posterior fornix of each patient for mycological culture examination. One dry swab was plated onto Sabouraud's medium, incubated for 48 hours at 37°C and then examined for colonies of *Candida* spp. The second swab was placed in *Trichomonas* culture medium (Medical Wire and Equipment, MW220). This was examined

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for colonies of *Candida* spp at once and after 48 hours' incubation at 37°C. Colonies of *Candida* spp were incubated in plasma at room temperature and examined microscopically for germ tubes. If germ tubes were present, the colonies were incubated at room temperature in corn meal agar and examined for chlamydospores daily for up to five days.

Either a single 500 mg clotrimazole tablet, or two 300 mg isoconazole tablets, allocated according to a randomisation code, were inserted into the vagina by the investigator using an applicator. Clotrimazole cream was given to the patients for the treatment of their sexual partners, and they were asked to abstain from sexual intercourse until after the first follow up visit.

Follow up examinations were carried out seven and 35 days after treatment. On both these occasions two specimens were taken for culture and the relevant physical signs and symptoms recorded. Patients were asked at day 7 to give their opinion on the acceptability of the preparation administered. Those found to be culture positive for *Candida* spp at day 7 were regarded as treatment failures. Adverse events or side effects were noted.

Results

Each treatment group contained 50 women, and the two groups are compared in table I. All patients were positive for *Candida* spp at the first visit. The results of mycological examination at the follow up visits are shown in table II. There was a very low default rate. One patient in the clotrimazole group and three in the isoconazole group failed to attend on day 35. Two patients treated with clotrimazole and one treated with isoconazole were excluded at day 35 as they had started additional antibiotic treatment. Two patients being treated with isoconazole developed severe side effects consisting of oedema and redness of the vulva and vagina. One of these was withdrawn from the trial and treated by painting the affected area with 1% aqueous solution of gentian violet. One

TABLE II Comparison of cure rates

	No (%) patients treated with:	
	Clotrimazole	Isoconazole
On day 7		
cured	50/50 (100)	47/50 (96)
failed	0	2/49 (4)
On day 35		
cured	34/47 (74)	35/45 (78)
recurred	12/47 (25)	9/45 (20)
failed	0	1/45 (2)

further patient given isoconazole complained of slight irritation and burning, as did two patients who had been treated with clotrimazole.

Discussion

Treatment with a single 500 mg clotrimazole tablet was found to be as effective as two 300 mg tablets of isoconazole in patients with acute vaginal candidosis. Although there were more patients cured with clotrimazole than isoconazole seven days after treatment, this difference was not statistically significant. One patient being treated with isoconazole remained positive for *Candida albicans* throughout treatment. The recurrence rates in this study were somewhat disappointing, though recurrence in one patient on clotrimazole was thought to be a result of reinfection by a new sexual partner. Improvement in clinical signs corresponded to negative results on mycological culture. This does not concur with the findings of Davidson and Mould,⁹ who found that the presence of yeasts in the vagina was not always associated with symptoms of vaginitis. Both treatment regimes were well tolerated, though two patients on isoconazole reported severe local oedema and erythema which resulted in one of them being withdrawn from the trial. These were the only two patients who found their treatment unacceptable.

Single dose regimens are an important development in the treatment of vaginal candidosis as they encourage patient compliance; total compliance can be ensured if the clinician inserts the tablet. This study has shown that a single tablet of clotrimazole is as effective as two tablets of isoconazole. There may be a place for single dose treatment in cases of recurrent vaginal candidosis where no obvious provoking cause can be found and other treatment regimens fail to provide a permanent cure. The patient could insert one tablet herself whenever her symptoms and signs recur.¹⁰

References

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TABLE I Comparison of treatment groups

Possible predisposing factors	Patients treated with:	
	Clotrimazole (n = 50) (Mean age 23.5 years)	Isoconazole (n = 50) (Mean age 26.4 years)
Previous vaginitis (%)	38	26
Accompanying diseases:		
Diabetes (%)	2	0
Iron deficiency (%)	2	2
Accompanying drugs:		
Oral steroids (%)	6	0
Oral contraceptives (%)	76	60

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